

WHAT IS CLAIMED IS:

1. A method for controlling a phenotype, the method comprising:

(i) providing a population of conjoint polynucleotide segments, wherein one or more conjoint polynucleotide segments comprise, encode or modulate a phenotype;

(ii) recombining or mutating the population of conjoint polynucleotide segments to produce a library of recombinant concatamers;

(iii) introducing the library of recombinant concatamers into a population of recipient cells or intracellular organelles; and,

(iv) identifying at least one recipient cell, intracellular organelle, or organism comprising a recipient cell, with a desired phenotype, thereby controlling the phenotype.

2. The method of claim 1, comprising controlling a complex phenotype by providing a population of conjoint polynucleotide segments, wherein one or more conjoint polynucleotide segments comprise, encode or modulate at least one element of a multigenic phenotype.

3. The method of claim 1, comprising controlling a complex phenotype by providing a population of conjoint polynucleotide segments, wherein one or more conjoint polynucleotide segments comprise, encode or modulate at least two elements of a multigenic phenotype.

4. The method of claim 1, comprising pre-selecting at least one polynucleotide sequence comprising conjoint polynucleotide segments by (a) introducing a population of random or selected conjoint polynucleotide segments into a plurality of recipient cells, (b) selecting at least one recipient cell, intracellular organelle, or organism comprising a recipient cell, with a desired phenotype, and (c) recovering at least one polynucleotide sequence comprising conjoint polynucleotide segments from the at least one recipient cell with a desired phenotype, thereby pre-selecting at least one polynucleotide sequence comprising conjoint polynucleotide segments.

5. The method of claim 1, comprising providing a population of conjoint polynucleotide segments comprising random polynucleotide segments.

6. The method of claim 1, comprising providing a population of conjoint polynucleotide segments comprising pre-selected polynucleotide segments.

5 7. The method of claim 6, wherein the polynucleotide segments are pre-selected for one or more encoded activities.

8. The method of claim 6, comprising identifying the pre-selected polynucleotide segments by computational analysis of at least one genomic or expressed sequence.

10 9. The method of claim 6, comprising identifying the pre-selected polynucleotide segments by expression analysis using at least one cDNA or oligonucleotide array.

10. The method of claim 6, comprising identifying the pre-selected polynucleotide segments by metabolic modeling and flux analysis.

15 11. The method of claim 6, comprising identifying the pre-selected polynucleotide segments by screening or selecting encoded peptides.

12. The method of claim 6, comprising identifying the pre-selected polynucleotide segments by Flow Cytometry.

20 13. The method of claim 6, comprising identifying the pre-selected polynucleotide segments by yeast two-hybrid analysis.

14. The method of claim 6, which pre-selected polynucleotide segments comprise one or more elements of a single metabolic or genetic pathway.

15. The method of claim 6, which pre-selected polynucleotide segments comprise elements of multiple metabolic or genetic pathways.

25 16. The method of claim 1, wherein the phenotype is regulated by at least one epigenetic mechanism.

17. The method of claim 16, wherein the epigenetic mechanism is selected from: chromatin silencing, methylation, maternal effects, regulation by cytoplasmic factors, antisense suppression, sense suppression, cosuppression, promoter alteration, homology-dependent mechanisms, aminoacylation, post-transcriptional gene silencing, and DNA recombination.

18. The method of claim 17, wherein the post-transcriptional gene silencing comprises post-translational silencing by a dominant negative inhibitor, a transdominant inhibitor, or a peptide inhibitor.

19. The method of claim 1, wherein the conjoint polynucleotide segments comprise one or more of: a genomic DNA, a cDNA, a sense-strand DNA, an antisense DNA, a DNA encoding a dominant negative protein variant or a transdominant protein variant, a DNA encoding a peptide modulator, a DNA encoding a 5-100 amino acid peptide, a DNA or RNA decoy, a viral DNA or RNA, an RNA, a sense-strand RNA, an antisense RNA, a tRNA, a ribozyme, an RNP, and a component of the RNA splicing machinery.

20. The method of claim 1, wherein the conjoint polynucleotide segments further comprise a vector.

21. The method of claim 20, wherein the vector comprises an episomal vector.

22. The method of claim 21, which vector is a plasmid, a virus, a provirus, a BAC, a YAC, a transposon, a bacteriophage, or a phagemid.

23. The method of claim 1, comprising introducing a plurality of conjoint polynucleotide segments into a recipient cell.

24. The method of claim 23, wherein the plurality of conjoint polynucleotide segments comprises members of a library of conjoint polynucleotide segments.

25. The method of claim 1, wherein the recipient cell is a bacterium, a yeast, a fungus, a plant cell, or an animal cell.

26. The method of claim 1, wherein the phenotype is selected from among: oil content or composition, fat content or composition, sugar content or composition, starch content or composition, protein content or composition, phytochemical content or composition, nutraceutical content or composition, yield, time
5 to maturity, growth rate, height at maturity, carbon-fixation rate, salt-tolerance, heat tolerance, cold tolerance, drought tolerance, water-tolerance, heavy metal tolerance, radiation tolerance, resistance to a chemical composition, disease resistance, insect resistance, parasite resistance, color, fluorescence, height, weight, density, toxicity, flavor, sweetness, bitterness, nutritional activity, or therapeutic activity.

27. The method of claim 1, wherein controlling the phenotype comprises modulating activity of one or more targets.

28. The method of claim 27, wherein the one or more targets comprise one or more enzymes.

29. The method of claim 1, comprising recursively recombining or
15 mutating the population of conjoint polynucleotide segments.

30. The method of claim 1, further comprising performing one or more additional diversity generating techniques prior to the recombining of step (ii).

31. The method of claim 1, wherein the recombinant concatamer is integrated into a chromosome of the recipient cell or organism comprising the recipient
20 cell.

32. The method of claim 1, wherein the recombinant concatamer is integrated into the DNA of an intracellular organelle.

33. The method of claim 1, further comprising recovering at least one recombinant concatamer from the cell, intracellular organelle or organism identified in
25 step (iv), and introducing the recombinant concatamer into a host cell.

34. The method of claim 33, wherein the recombinant concatamer comprises an episomal vector.

35. The method of claim 34, wherein the recombinant concatamer is integrated into a chromosome.

36. The method of claim 33, further comprising regenerating at least one multicellular organism comprising the host cell.

5 **37.** The method of claim 33, wherein the host cell is a bacterial cell, a fungal cell, a plant cell or an animal cell.

38. The method of claim 1, further comprising isolating at least one genetic element corresponding to a subsequence of the conjoint polynucleotide segments or recombinant concatamer.

10 **39.** The method of claim 38, further comprising:
recombining or mutating the at least one isolated genetic element, thereby producing a library of isolated gene homologues, and
selecting at least one gene homologue with a desired property.

15 **40.** The method of claim 1, wherein the intracellular organelle comprises a mitochondria or a chloroplast.

41. A method for controlling a phenotype, the method comprising:
(i) providing a library of nucleic acids, which library of nucleic acids comprises a plurality of conjoint polynucleotide segments operably linked to at least one transcription regulatory sequence, which conjoint polynucleotide segments alter
20 expression or activity of at least one component of an endogenous phenotype;
(ii) introducing the library of nucleic acids into a population of recipient cells or intracellular organelles; and
(iii) identifying at least one recipient cell, intracellular organelle or organism comprising a recipient cell, with a desired phenotype, thereby controlling the
25 phenotype.

42. The method of claim 41, comprising controlling a complex phenotype by providing a plurality of conjoint polynucleotide segments that alter expression or activity of at least one component of a multigenic phenotype.

43. The method of claim 41, comprising controlling a complex phenotype by providing a plurality of conjoint polynucleotide segments that alter expression or activity of at least two components of a multigenic phenotype.

5 44. The method of claim 41, further comprising recombining or mutating a polynucleotide comprising conjoint polynucleotide segments, which polynucleotide confers the desired phenotype on the recipient cell, intracellular organelle or organism comprising the recipient cell identified in step (iii).

10 45. The method of claim 41, comprising pre-selecting at least one nucleic acid comprising conjoint polynucleotide segments by (a) introducing a population of random or selected conjoint polynucleotide segments into a plurality of recipient cells, (b) selecting at least one recipient cell, intracellular organelle, or organism comprising a recipient cell, with a desired phenotype, and (c) recovering at least one nucleic acid comprising conjoint polynucleotide segments from the at least one recipient cell with a desired phenotype, thereby pre-selecting at least one nucleic acid comprising conjoint
15 polynucleotide segments.

46. The method of claim 41, comprising providing a plurality of conjoint polynucleotide segments comprising random polynucleotide segments.

47. The method of claim 41, comprising a plurality of conjoint polynucleotide segments comprising pre-selected polynucleotide segments.

20 48. The method of claim 47, wherein the polynucleotide segments are pre-selected for one or more encoded activities.

49. The method of claim 47, comprising identifying the pre-selected polynucleotide segments by computational analysis of at least one genomic or expressed sequence.

25 50. The method of claim 47, comprising identifying the pre-selected polynucleotide segments by expression analysis using at least one cDNA or oligonucleotide array.

51. The method of claim 47, comprising identifying the pre-selected polynucleotide segments by metabolic modeling and flux analysis.

52. The method of claim 47, comprising identifying the pre-selected polynucleotide segments by screening or selecting encoded peptides.

5 **53.** The method of claim 47, comprising identifying the pre-selected polynucleotide segments by Flow Cytometry.

54. The method of claim 47, comprising identifying the pre-selected polynucleotide segments by yeast two-hybrid analysis.

10 **55.** The method of claim 47, which pre-selected polynucleotide segments comprise one or more elements of a single metabolic or genetic pathway.

56. The method of claim 47, which pre-selected polynucleotide segments comprise elements of multiple metabolic or genetic pathways.

57. The method of claim 41, wherein the phenotype is regulated by at least one epigenetic mechanism.

15 **58.** The method of claim 57, wherein the epigenetic mechanism is selected from: chromatin silencing, methylation, maternal effects, regulation by cytoplasmic factors, antisense suppression, sense suppression, cosuppression, promoter alteration, homology-dependent mechanisms, aminoacylation, post-transcriptional gene silencing, and DNA recombination.

20 **59.** The method of claim 58, wherein the post-transcriptional gene silencing comprises post-translational silencing by a dominant negative inhibitor, a transdominant inhibitor, or a peptide inhibitor.

25 **60.** The method of claim 41, wherein the conjoint polynucleotide segments comprise one or more of: a genomic DNA, a cDNA, a sense-strand DNA, an antisense DNA, a DNA encoding a dominant negative protein variant or a transdominant protein variant, a DNA encoding a peptide modulator, a DNA encoding a 5-100 amino acid peptide, a DNA or RNA decoy, a viral DNA or RNA, an RNA, a sense-strand RNA,

an antisense RNA, a tRNA, a ribozyme, an RNP, and a component of the RNA splicing machinery.

61. The method of claim 41, wherein the conjoint polynucleotide segments further comprise a vector.

5 **62.** The method of claim 61, wherein the vector comprises an episomal vector.

63. The method of claim 62, which vector is a plasmid, a virus, a provirus, a BAC, a YAC, a transposon, a bacteriophage, or a phagemid.

10 **64.** The method of claim 41, further comprising recovering at least one nucleic acid comprising conjoint polynucleotide segments from the cell, intracellular organelle or organism identified in step (iii), and introducing the nucleic acid into a host cell.

65. The method of claim 64, wherein the nucleic acid is integrated into a chromosome.

15 **66.** The method of claim 64, further comprising regenerating at least one multicellular organism comprising the host cell.

67. The method of claim 64, wherein the host cell is a bacterial cell, a fungal cell, a plant cell or an animal cell.

20 **68.** The method of claim 41, wherein the intracellular organelle comprises a mitochondria or a chloroplast.

69. The method of claim 41, wherein the phenotype is selected from among: oil content or composition, fat content or composition, sugar content or composition, starch content or composition, protein content or composition, phytochemical content or composition, nutraceutical content or composition, yield, time to maturity, growth rate, height at maturity, carbon-fixation rate, salt-tolerance, heat tolerance, cold tolerance, drought tolerance, water-tolerance, heavy metal tolerance, radiation tolerance, resistance to a chemical composition, disease resistance, insect

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resistance, parasite resistance, color, fluorescence, height, weight, density, toxicity, flavor, sweetness, bitterness, nutritional activity, or therapeutic activity.

70. The method of claim 41, wherein controlling the phenotype comprises modulating activity of one or more targets.

5 **71.** The method of claim 70, wherein the one or more targets comprise one or more enzymes.

72. The method of claim 41, further comprising isolating at least one genetic element corresponding to a subsequence of the conjoint polynucleotide segments or recombinant concatamer.

10 **73.** The method of claim 72, further comprising:
recombining or mutating the at least one isolated genetic element, thereby producing a library of isolated gene homologues, and
selecting at least one gene homologue with a desired property.

15 **74.** A method for controlling a complex phenotype, the method comprising:
(i) providing a library of nucleic acids, which nucleic acids comprise one or more polynucleotide segments operably linked to at least one transcription regulatory sequence;

20 (ii) introducing the library of nucleic acids into a population of recipient cells or intracellular organelles, whereby subsets of two or more members of the library, which subsets alter expression or activity of one or more components of a multigenic phenotype, are introduced into a plurality of the recipient cells or organelles; and

25 (iii) identifying at least one recipient cell, intracellular organelle or organism comprising a recipient cell, with a desired phenotype, thereby controlling the complex phenotype.

75. The method of claim 74, comprising introducing the library of nucleic acids into a population of recipient cells or intracellular organelles, whereby subsets of two or more members of the library, which subsets alter expression or activity

of two or more components of a multigenic phenotype, are introduced into a plurality of the recipient cells or organelles.

76. The method of claim 74, comprising providing a library of random polynucleotide segments.

5 **77.** The method of claim 74, comprising providing a library of pre-selected polynucleotide segments.

10 **78.** The method of claim 77, comprising pre-selecting at least one polynucleotide segment by (a) introducing a population of random or selected polynucleotide segments into a plurality of recipient cells, (b) selecting at least one recipient cell, intracellular organelle, or organism comprising a recipient cell, with a desired phenotype, and (c) recovering one or more polynucleotide segments from the at least one recipient cell with a desired phenotype, thereby pre-selecting one or more polynucleotide segments.

15 **79.** The method of claim 77, wherein the polynucleotide segments are pre-selected for one or more encoded activities.

80. The method of claim 77, comprising identifying the pre-selected polynucleotide segments by computational analysis of at least one genomic or expressed sequence.

20 **81.** The method of claim 77, comprising identifying the pre-selected polynucleotide segments by expression analysis using at least one cDNA or oligonucleotide array.

82. The method of claim 77, comprising identifying the pre-selected polynucleotide segments by metabolic modeling and flux analysis.

25 **83.** The method of claim 77, comprising identifying the pre-selected polynucleotide segments by screening or selecting encoded peptides.

84. The method of claim 77, comprising identifying the pre-selected polynucleotide segments by Flow Cytometry.

85. The method of claim 77, comprising identifying the pre-selected polynucleotide segments by yeast two-hybrid analysis.

86. The method of claim 77, which pre-selected polynucleotide segments comprise one or more elements of a single metabolic or genetic pathway.

5 **87.** The method of claim 77, which pre-selected polynucleotide segments comprise elements of multiple metabolic or genetic pathways.

88. The method of claim 74, wherein the phenotype is regulated by at least one epigenetic mechanism.

10 **89.** The method of claim 88, wherein the epigenetic mechanism is selected from: chromatin silencing, methylation, maternal effects, regulation by cytoplasmic factors, antisense suppression, sense suppression, cosuppression, promoter alteration, homology-dependent mechanisms, aminoacylation, post-transcriptional gene silencing, and DNA recombination.

15 **90.** The method of claim 89, wherein the post-transcriptional gene silencing comprises post-translational silencing by a dominant negative inhibitor, a transdominant inhibitor, or a peptide inhibitor.

20 **91.** The method of claim 74, the polynucleotide segments comprising one or more of: a genomic DNA, a cDNA, a sense-strand DNA, an antisense DNA, a DNA encoding a dominant negative protein variant or a transdominant protein variant, a DNA encoding a peptide modulator, a DNA encoding a 5-100 amino acid peptide, a DNA or RNA decoy, a viral DNA or RNA, an RNA, a sense-strand RNA, an antisense RNA, a tRNA, a ribozyme, an RNP, and a component of the RNA splicing machinery.

92. The method of claim 74, wherein the nucleic acids further comprise a vector.

25 **93.** The method of claim 92, wherein the vector comprises an episomal vector.

94. The method of claim 93, which vector is a plasmid, a virus, a provirus, a BAC, a YAC, a transposon, a bacteriophage, or a phagemid.

95. The method of claim 74, wherein the recipient cells comprise a bacterium, a yeast, a fungus, a plant cell, or an animal cell.

5 **96.** The method of claim 74, wherein the phenotype is selected from among: oil content or composition, fat content or composition, sugar content or composition, starch content or composition, protein content or composition, phytochemical content or composition, nutraceutical content or composition, yield, time to maturity, growth rate, height at maturity, carbon-fixation rate, salt-tolerance, heat
10 tolerance, cold tolerance, drought tolerance, water-tolerance, heavy metal tolerance, radiation tolerance, resistance to a chemical composition, disease resistance, insect resistance, parasite resistance, color, fluorescence, height, weight, density, toxicity, flavor, sweetness, bitterness, nutritional activity, or therapeutic activity.

97. The method of claim 74, wherein controlling the phenotype
15 comprises modulating activity of one or more targets.

98. The method of claim 97, wherein the one or more targets comprise one or more enzymes.

99. The method of claim 74, further comprising identifying or recovering
20 one or more members of the library from the cells with a desired phenotype identified in step (iii).

100. The method of claim 99, further comprising recombining or mutating the one or more identified or recovered members of the library, thereby producing at least one recombinant polynucleotide segment.

25 **101.** The method of claim 100, comprising recursively recombining or mutating the one or more members of the library.

102. The method of claim 100, further comprising introducing the at least one recombinant polynucleotide segment into a host cell.

103. The method of claim 102, wherein the at least one recombinant polynucleotide segment is integrated into a chromosome.

104. The method of claim 102, further comprising regenerating at least one multicellular organism comprising the host cell.

5 **105.** The method of claim 102, wherein the host cell is a bacterial cell, a fungal cell, a plant cell or an animal cell.

106. The method of claim 99, further comprising isolating at least one genetic element corresponding to a library member or recombinant polynucleotide segment.

10 **107.** The method of claim 106, further comprising:
recombining or mutating the at least one isolated genetic element, thereby
producing a library of isolated gene homologues, and
selecting at least one gene homologue with a desired property.

15 **108.** The method of claim 74, wherein the intracellular organelle
comprises a mitochondria or a chloroplast.

109. A method of modulating activity of one or more targets, the method comprising:

20 (a) providing a library of polynucleotide segments encoding a plurality of
peptides, which peptides are pre-selected for one or more desired properties, which
desired properties are the same or different between peptides;

 (b) joining the pre-selected polynucleotide segments to generate a
population of conjoint polynucleotide segments, which conjoint polynucleotide segments
are operably linked to at least one transcription regulatory sequence;

25 (c) expressing one or more of the conjoint polynucleotide segments in
vitro or in vivo, thereby producing one or more multi-peptides, which multi-peptides
comprise a plurality of peptide segments, which segments are optionally joined by a
linker sequence;

(d) identifying one or more conjoint polynucleotide segments encoding a multi-peptide, which multi-peptide comprises at least one peptide capable of modulating activity of one or more targets.

110. The method of claim 109, further comprising:

(e) recombining or mutating the one or more conjoint polynucleotide segments encoding a multi-peptide one or more times to produce a library of recombinant concatamers;

(f) expressing one or more recombinant concatamers; and,

(g) identifying at least one recombinant concatamer with a desired property.

111. The method of claim 110, comprising recursively recombining or mutating the one or more conjoint polynucleotide segments.

112. The method of claim 110, comprising performing one or more additional diversity generating techniques prior to recombining the one or more conjoint polynucleotide segments.

113. The method of claim 109, wherein the peptides comprise different amino acid sequences.

114. The method of claim 109, wherein the peptides comprise peptide modulators.

115. The method of claim 109, wherein the peptide modulators comprise peptide inhibitors.

116. The method of claim 109, wherein the peptides modulate an enzyme.

117. The method of claim 109, wherein the polynucleotide segments comprise synthetic oligonucleotides.

118. The method of claim 109, wherein the polynucleotide segments are produced by a polymerase chain reaction (PCR).

119. The method of claim 109, wherein the library comprises random polynucleotide segments.

120. The method of claim 109, wherein the library comprises pre-selected polynucleotide segments.

5 **121.** The method of claim 109, comprising pre-selecting the library of polynucleotide segments by (a) introducing a plurality of random, partially randomized or designed polynucleotide segments into a population of recipient cells, (b) selecting one or more recipient cells with a desired phenotype, and (c) recovering at least one polynucleotide segment from the one or more recipient cells with a desired phenotype,
10 thereby pre-selecting the library of polynucleotide segments.

122. The method of claim 121, comprising introducing the plurality polynucleotide segments into a population of recipient cells, wherein the polynucleotide segments are expressed as fusion proteins on the surface of the recipient cell.

123. The method of claim 122, comprising selecting one or more recipient
15 cells expressing a fusion protein that binds to a labeled target.

124. The method of claim 109, wherein the polynucleotide segments are pre-selected for one or more encoded activities.

125. The method of claim 109, comprising identifying the pre-selected polynucleotide segments by computational analysis of at least one genomic or expressed
20 sequence.

126. The method of claim 109, comprising identifying the pre-selected polynucleotide segments by expression analysis using at least one cDNA or oligonucleotide array.

127. The method of claim 109, comprising identifying the pre-selected
25 polynucleotide segments by metabolic modeling and flux analysis.

128. The method of claim 109, comprising identifying the pre-selected polynucleotide segments by screening or selecting encoded peptides.

129. The method of claim 109, comprising identifying the pre-selected polynucleotide segments by phage display, bacterial display, yeast display, or ribosomal display.

130. The method of claim 109, comprising identifying the pre-selected polynucleotide segments by Flow Cytometry.

131. The method of claim 109, comprising identifying the pre-selected polynucleotide segments by yeast two-hybrid analysis.

132. The method of claim 109, comprising providing the library of pre-selected peptides by:

10 (a) providing a library of nucleic acids encoding fusion polypeptides, which fusion polypeptides are capable of displaying one or more variable peptide moiety in vitro or in vivo;

(b) expressing the fusion polypeptides such that the one or more variable peptide moieties is displayed in vitro or in vivo; and,

15 (c) identifying a plurality of variable peptide moieties with a desired property, thereby producing a library of pre-selected peptides.

133. The method of claim 109, the polynucleotide segments comprising one or more of: a genomic DNA, a cDNA, a sense-strand DNA, an antisense DNA, a DNA encoding a dominant negative protein variant or a transdominant protein variant, a DNA encoding a peptide modulator, a DNA encoding a 5-100 amino acid peptide, a DNA or RNA decoy, a viral DNA or RNA, an RNA, a sense-strand RNA, an antisense RNA, a tRNA, a ribozyme, an RNP, and a component of the RNA splicing machinery.

134. The method of claim 109, wherein the conjoint polynucleotide segments further comprise a vector.

25 135. The method of claim 134, wherein the vector comprises an episomal vector.

136. The method of claim 135, which vector is a plasmid, a virus, a provirus, a BAC, a YAC, a transposon, a bacteriophage, or a phagemid.

137. The method of claim 109, wherein modulating activity of the one or more targets modifies a phenotype selected from among: oil content or composition, fat content or composition, sugar content or composition, starch content or composition, protein content or composition, phytochemical content or composition, nutraceutical
5 content or composition, yield, time to maturity, growth rate, height at maturity, carbon-fixation rate, salt-tolerance, heat tolerance, cold tolerance, drought tolerance, water-tolerance, heavy metal tolerance, radiation tolerance, resistance to a chemical composition, disease resistance, insect resistance, parasite resistance, color, fluorescence, height, weight, density, toxicity, flavor, sweetness, bitterness, nutritional activity, or
10 therapeutic activity.

138. The method of claim 109, wherein the one or more targets comprise one or more enzymes.

139. The method of claim 138, wherein the one or more targets comprise a class of enzymes.

15 140. The method of claim 138, wherein the one or more targets comprise at least two different enzymes, which different enzymes are modulated by one or more peptide components of the multi-peptide.

141. The method of claim 138, wherein the one or more targets comprise one or more enzymes with multiple functions, which multiple functions are modulated by
20 one or more peptide components of the multi-peptide.

142. The method of claim 109, wherein at least one peptide modulates activity by binding to the target.

143. The method of claim 142, wherein the at least one peptide binds to a catalytic site of the target.

25 144. The method of claim 109, comprising modulating one or more target selected from among intracellular molecules, extracellular molecules and cell-surface molecules.

145. The method of claim 109, wherein modulating activity of a target comprises one or more of: altering target binding to a substrate, altering catalytic activity of a target, altering anabolic activity of a target, altering stability of a target, altering substrate specificity of a target, altering the ability of a target to function in a selected environment.

146. The method of claim 145, comprising modulating a plurality of targets comprising a multiple members of a class of related enzymes.

147. The method of claim 146, wherein the class of related enzymes comprise proteases, lipases, esterases, hydrolases or amylases.

148. The method of claim 109, comprising joining the pre-selected polynucleotide segments by a ligation reaction or by a polymerase chain reaction (PCR).

149. The method of claim 109, wherein the polynucleotide segments encode pre-selected peptides about 5 to about 100 amino acids in length.

150. The method of claim 109, wherein the linker sequence comprises a polynucleotide encoding a peptide subject to proteolytic cleavage.

151. The method of claim 109, comprising expressing the one or more conjoint polynucleotide segments by one or more of in vitro transcription, in vitro translation, or ribosomal display.

152. The method of claim 109, comprising expressing the one or more conjoint polynucleotide segments by introducing a the plurality of conjoint polynucleotide segments into a population of recipient cells.

153. The method of claim 152, wherein the recipient cells comprise a bacterium, a yeast, a fungus, a plant cell, or an animal cell.

154. A method of producing a library of pre-selected peptides, the method comprising:

(a) providing a library of nucleic acids encoding fusion polypeptides, which fusion polypeptides are capable of displaying one or more variable peptide moiety in vitro or in vivo;

5 (b) expressing the fusion polypeptides such that the one or more variable peptide moieties is displayed in vitro or in vivo; and,

(c) identifying a plurality of variable peptide moieties with a desired property, thereby producing a library of pre-selected peptides.

155. The method of claim 154, wherein the library of pre-selected peptides comprises in excess of about 100 different members.

10 **156.** The method of claim 154, wherein the library of pre-selected peptides comprises in excess of about 1000, in excess of about 10,000, in excess of about 100,000 or in excess of about 1,000,000 different members.

157. The method of claim 154, further comprising recovering one or more nucleic acids encoding the pre-selected peptides.

15 **158.** The method of claim 154, further comprising joining a plurality of polynucleotide segments encoding the variable peptide moieties, thereby producing one or more conjoint polynucleotide segments encoding a multipeptide.

159. The method of claim 158, recombining or mutating the one or more conjoint polynucleotide segments encoding a multipeptide to produce a library of
20 recombinant concatamers.

160. The method of claim 159, further comprising identifying at least one recombinant concatamer with a desired property.

161. The method of claim 154, comprising displaying the variable peptide moieties by a ribosomal display method, a phage display method, a bacterial display
25 method or a yeast display method.

162. The method of claim 161, comprising displaying the variable peptide moieties as fusions with a bacterial cell surface protein.

163. The method of claim 162, wherein the fusion polypeptide comprises a bacterial OmpA polypeptide.

164. The method of claim 161, comprising detecting one or more variable peptide moieties with a desired property by binding to a labeled target.

5 **165.** The method of claim 164, wherein the labeled target comprises an enzyme.

166. The method of claim 164, comprising detecting the one or more variable peptide moieties with a desired property by Flow Cytometry.

10 **167.** A library of pre-selected peptide produced by the method of claim 154.

168. A library of nucleic acids, which library of nucleic acids comprises a plurality of conjoint polynucleotide segments operably linked to at least one transcription regulatory sequence, which conjoint polynucleotide segments alter expression of one or more components of an endogenous phenotype.

15 **169.** The library of claim 168, wherein the conjoint polynucleotide segments alter expression of multiple components of an endogenous phenotype.

170. The library of claim 168, wherein the endogenous phenotype comprises a multigenic phenotype.

20 **171.** The library of claim 168, the polynucleotide segments comprising a plurality of sense or antisense sequences comprising all or part of one or more of a promoter, an enhancer, and a structural gene.

172. The library of claim 171, wherein the structural gene encodes a transcription regulatory factor, an enzyme, a receptor, a hormone, or a signaling peptide or polypeptide.

25 **173.** A library comprising the population of conjoint polynucleotide segments of claim 1, 41 or 109.

174. The library of recombinant concatamers of claim 173, the recombinant concatamers comprising one or more of: a genomic DNA, a cDNA, a sense-strand DNA, an antisense DNA, a DNA encoding a dominant negative protein variant or a transdominant protein variant, a DNA encoding a peptide modulator, a DNA encoding a 5-100 amino acid peptide, a DNA or RNA decoy, a viral DNA or RNA, an RNA, a sense-strand RNA, an antisense RNA, a tRNA, a ribozyme, an RNP, and a component of the RNA splicing machinery.

175. The library of claim 173, the recombinant concatamers comprising a plurality of sense or antisense sequences comprising all or part of one or more of a promoter, an enhancer, and a structural gene.

176. The library of claim 173, wherein the structural gene encodes a transcription regulatory factor, an enzyme, a receptor, a hormone, or a signaling peptide or polypeptide.

177. The library of recombinant concatamers of claim 1, 41 or 110.

178. The library of recombinant concatamers of claim 178, the recombinant concatamers comprising one or more of: a genomic DNA, a cDNA, a sense-strand DNA, an antisense DNA, a DNA encoding a dominant negative protein variant or a transdominant protein variant, a DNA encoding a peptide modulator, a DNA encoding a 5-100 amino acid peptide, a DNA or RNA decoy, a viral DNA or RNA, an RNA, a sense-strand RNA, an antisense RNA, a tRNA, a ribozyme, an RNP, and a component of the RNA splicing machinery.

179. The library of claim 178, the recombinant concatamers comprising a plurality of sense or antisense sequences comprising all or part of one or more of a promoter, an enhancer, and a structural gene.

180. The library of claim 178, wherein the structural gene encodes a transcription regulatory factor, an enzyme, a receptor, a hormone, or a signaling peptide or polypeptide.

181. The vector of claim 21, 62 and 135.

182. The vector of claim 181, which vector is a plasmid, a virus, a provirus, a BAC, a YAC, a transposon, a bacteriophage, or a phagemid.

183. A cell or an organism comprising a cell produced by the method of claim 1, 41 or 74.

5 **184.** The cell of claim 183, wherein the cell comprises a bacterial cell, a fungal cell, a plant cell or an animal cell.

185. The organism of claim 183, wherein the organism is a bacterium, a yeast, a fungus, a plant or an animal.

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